

**APPENDIX B: CLAIM AMENDMENTS**

10. (Amended) The isolated human antibody or antigen-binding portion thereof according to [any one of claims 1-9] claim 1, wherein said antibody or antigen binding portion thereof has HIV-1<sub>SF162</sub> neutralizing activity.

11. (Amended) The isolated human antibody or antigen-binding portion thereof according to [any one of claims 1-9] claim 1, wherein said antibody or antigen binding portion thereof recognizes a linear epitope on a V1 domain of HIV-1<sub>SF162</sub> gp120.

16. (Amended) The isolated human antibody or antigen-binding portion thereof according to [any one of claims 1-9 or 12-15] claim 1, wherein the human antibody is a human monoclonal antibody.

23. (Amended) The isolated human antibody or antigen-binding portion thereof according to claim 1, wherein said human antibody comprises a heavy chain of [a] the human antibody according to claim 20.

27. (Amended) A host cell transformed with [a] the nucleic acid according to claim 24.

35. (Amended) The isolated human antibody or antigen-binding portion thereof according to [any one of claims 31-34] claim 31, wherein the human antibody is a human monoclonal antibody.

38. (Amended) The isolated human antibody or antigen-binding portion thereof according to [any one of claims 31-34] claim 31, wherein said human antibody, wherein said antibody does not bind to a gp120 of HIV-1 IIIB, HBX2, HBX2d or BH10.

39. (Amended) A hybridoma cell line designated 8.22.2 and having ATCC Accession Number PTA-4007.

43. (Amended) The isolated human monoclonal antibody or antigen-binding portion thereof according to claim [31] 35, wherein said human monoclonal antibody comprises a heavy chain of the antibody according to claim 40.

44. (Amended) The isolated human monoclonal antibody or antigen-binding portion thereof according to claim

[31] 35, wherein said human antibody comprises a heavy chain CDR1, CDR2 and CDR3 from the antibody according to claim 40.

58. (Amended) A hybridoma cell line selected from the group consisting of: cell line 8.27.3 (ATCC Accession Number PTA-3009) and cell line 8E11/A8 (ATCC Accession Number PTA-4012).

64. (Amended) The isolated human monoclonal antibody or antigen-binding portion thereof according to [any one of claims 56, 57 or 59-63] claim 56, wherein said antibody has HIV-1 neutralizing activity.

78. (Amended) The isolated human monoclonal antibody or antigen-binding portion thereof according any one of claims [17-18] 16, 35 or 56, wherein the antibody or portion thereof is an immunoglobulin G (IgG), an IgM, an IgE, an IgA or an IgD molecule, or is derived therefrom.

85. (Amended) The isolated human monoclonal antibody or antigen-binding portion thereof according to claim 16, 35 or 56 wherein the antibody or portion thereof is labeled.

88. (Amended) The isolated human monoclonal antibody or antigen-binding portion thereof according to [any one of claims 85-86] claim 85, wherein the label is selected from the group consisting of a radiolabel, an enzyme label, a toxin and a magnetic agent.

91. (Amended) The isolated human monoclonal antibody or antigen-binding portion thereof according to claim 16, 35 or 56 wherein the antibody is a single chain antibody.

94. (Amended) The isolated human monoclonal antibody or antigen-binding portion thereof according to claim 16, 35 or 56 wherein the antibody is a chimeric antibody.

97. (Amended) The chimeric antibody according to claim [96] 94, wherein the chimeric antibody comprises framework regions and CDR regions from different human monoclonal antibodies.

102. (Amended) The chimeric antibody according to claim [96] 94, wherein the chimeric antibody is bispecific.

104. (Amended) The isolated human monoclonal antibody or antigen-binding portion thereof according to claim

16, 35 or 56 wherein the antibody or portion thereof is derivatized.

107. (Amended) The isolated human monoclonal antibody or antigen-binding portion thereof according to claim [106] 104, wherein the antibody or portion thereof is derivatized with polyethylene glycol, at least one methyl or ethyl group or at least one carbohydrate moiety.

109. (Amended) A composition comprising [the antibody or portion thereof according to any one of claims 1-18, 20-23, 30-38, 40-44, 51-57, 59-70 or 77] an isolated human antibody or antigen-binding portion thereof selected from the group consisting of

an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein and that has HIV-1 neutralizing activity, wherein said antibody or antigen-binding portion thereof recognizes a epitope on a V1/V2 domain of HIV-1 gp120, wherein said epitope is dependent on the presence of a sequence in the V1 loop;

an isolated human monoclonal antibody produced by the hybridoma cell line selected from the group consisting of: cell line 35D10/D2 (ATCC Accession Number PTA-3001), cell line 40H2/C7 (ATCC Accession Number PTA-3006), cell line 43A3/E4

(ATCC Accession Number PTA-3005), cell line 43C7/B9 (ATCC Accession Number PTA-3007), cell line 45D1/B7 (ATCC Accession Number PTA-3002), cell line 46E3/E6 (ATCC Accession Number PTA-3008), cell line 58E1/B3 (ATCC Accession Number PTA-3003), cell line 64B9/A6 (ATCC Accession Number PTA-3004), cell line 8.22.2 (ATCC Accession Number PTA-4007), and cell line 8.27.3 (ATCC Accession Number PTA-4012), or an antigen-binding portion thereof;

an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein and that has HIV-1 neutralizing activity, wherein said antibody or antigen-binding portion thereof recognizes a epitope on a V1/V2 domain of HIV-1 gp120, wherein said antibody or antigen binding portion thereof recognizes a linear epitope on a V2 domain of HIV-1 gp120; and

an isolated human monoclonal antibody or antigen-binding portion thereof that specifically binds to an epitope on a V3 region of HIV-1 gp120, wherein said antibody binds to an epitope on the V3 region of HIV-1, and wherein said antibody does not specifically bind to a peptide consisting of SEQ ID NO: 9,

and a pharmaceutically acceptable carrier.

110. (Amended) The composition according to claim 109 further comprising [at least one] one or more additional therapeutic agents.

112. (Amended) A kit comprising a container comprising [the antibody or portion thereof according to any one of claims 1-18, 20-23, 30-38, 40-44, 51-57, 59-70 or 77,] an isolated human antibody or antigen-binding portion thereof selected from the group consisting of

an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein and that has HIV-1 neutralizing activity, wherein said antibody or antigen-binding portion thereof recognizes a epitope on a V1/V2 domain of HIV-1 gp120, wherein said epitope is dependent on the presence of a sequence in the V1 loop;

an isolated human monoclonal antibody produced by the hybridoma cell line selected from the group consisting of: cell line 35D10/D2 (ATCC Accession Number PTA-3001), cell line 40H2/C7 (ATCC Accession Number PTA-3006), cell line 43A3/E4 (ATCC Accession Number PTA-3005), cell line 43C7/B9 (ATCC Accession Number PTA-3007), cell line 45D1/B7 (ATCC Accession Number PTA-3002), cell line 46E3/E6 (ATCC Accession Number PTA-3008), cell line 58E1/B3 (ATCC Accession Number PTA-3003), cell line 64B9/A6 (ATCC Accession Number PTA-3004), cell line

8.22.2 (ATCC Accession Number PTA-4007), and cell line 8.27.3 (ATCC Accession Number PTA-4012), or an antigen-binding portion thereof;

an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein and that has HIV-1 neutralizing activity, wherein said antibody or antigen-binding portion thereof recognizes a epitope on a V1/V2 domain of HIV-1 gp120, wherein said antibody or antigen binding portion thereof recognizes a linear epitope on a V2 domain of HIV-1 gp120; and

an isolated human monoclonal antibody or antigen-binding portion thereof that specifically binds to an epitope on a V3 region of HIV-1 gp120, wherein said antibody binds to an epitope on the V3 region of HIV-1, and wherein said antibody does not specifically bind to a peptide consisting of SEQ ID NO: 9,

and a pharmaceutically acceptable carrier therefor.

114. (Amended) The kit according to [any one of claims 112-113] claim 112, further comprising another anti-viral agent, an immunomodulator or an immunostimulator, or any combination thereof.



115. (Amended) A method for treating a subject with an HIV-1 infection comprising the step of administering [an antibody according to any one of claims 1-18, 20-23, 30-38, 40-44, 51-57, 59-70 or 77, or an antigen-binding portion thereof] an isolated human antibody or antigen-binding portion thereof selected from the group consisting of

an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein and that has HIV-1 neutralizing activity, wherein said antibody or antigen-binding portion thereof recognizes an epitope on a V1/V2 domain of HIV-1 gp120, wherein said epitope is dependent on the presence of a sequence in the V1 loop;

an isolated human monoclonal antibody produced by the hybridoma cell line selected from the group consisting of: cell line 35D10/D2 (ATCC Accession Number PTA-3001), cell line 40H2/C7 (ATCC Accession Number PTA-3006), cell line 43A3/E4 (ATCC Accession Number PTA-3005), cell line 43C7/B9 (ATCC Accession Number PTA-3007), cell line 45D1/B7 (ATCC Accession Number PTA-3002), cell line 46E3/E6 (ATCC Accession Number PTA-3008), cell line 58E1/B3 (ATCC Accession Number PTA-3003), cell line 64B9/A6 (ATCC Accession Number PTA-3004), cell line 8.22.2 (ATCC Accession Number PTA-4007), and cell line 8.27.3 (ATCC Accession Number PTA-4012), or an antigen-binding portion thereof;

an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein and that has HIV-1 neutralizing activity, wherein said antibody or antigen-binding portion thereof recognizes a epitope on a V1/V2 domain of HIV-1 gp120, wherein said antibody or antigen binding portion thereof recognizes a linear epitope on a V2 domain of HIV-1 gp120; and

an isolated human monoclonal antibody or antigen-binding portion thereof that specifically binds to an epitope on a V3 region of HIV-1 gp120, wherein said antibody binds to an epitope on the V3 region of HIV-1, and wherein said antibody does not specifically bind to a peptide consisting of SEQ ID NO: 9.

116. (Amended) A method for preventing or inhibiting HIV-1 infection in a subject comprising the step of administering [an antibody according to any one of claims 1-18, 20-23, 30-38, 40-44, 51-57, 59-70 or 77, or an antigen-binding portion thereof] an isolated human antibody or antigen-binding portion thereof selected from the group consisting of

an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein and that has HIV-1 neutralizing activity, wherein said antibody or

antigen-binding portion thereof recognizes a epitope on a V1/V2 domain of HIV-1 gp120, wherein said epitope is dependent on the presence of a sequence in the V1 loop;

an isolated human monoclonal antibody produced by the hybridoma cell line selected from the group consisting of: cell line 35D10/D2 (ATCC Accession Number PTA-3001), cell line 40H2/C7 (ATCC Accession Number PTA-3006), cell line 43A3/E4 (ATCC Accession Number PTA-3005), cell line 43C7/B9 (ATCC Accession Number PTA-3007), cell line 45D1/B7 (ATCC Accession Number PTA-3002), cell line 46E3/E6 (ATCC Accession Number PTA-3008), cell line 58E1/B3 (ATCC Accession Number PTA-3003), cell line 64B9/A6 (ATCC Accession Number PTA-3004), cell line 8.22.2 (ATCC Accession Number PTA-4007), and cell line 8.27.3 (ATCC Accession Number PTA-4012), or an antigen-binding portion thereof;

an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein and that has HIV-1 neutralizing activity, wherein said antibody or antigen-binding portion thereof recognizes a epitope on a V1/V2 domain of HIV-1 gp120, wherein said antibody or antigen binding portion thereof recognizes a linear epitope on a V2 domain of HIV-1 gp120; and

an isolated human monoclonal antibody or antigen-binding portion thereof that specifically binds to an epitope on a V3

region of HIV-1 gp120, wherein said antibody binds to an epitope on the V3 region of HIV-1, and wherein said antibody does not specifically bind to a peptide consisting of SEQ ID NO: 9.

118. (Amended) A method for inhibiting HIV-1 virus binding to a T cell comprising the step of contacting said virus with [an antibody according to any one of claims 1-18, 20-23, 30-38, 40-44, 51-57, 59-70 or 77, or an antigen-binding portion thereof] an isolated human antibody or antigen-binding portion thereof selected from the group consisting of

an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein and that has HIV-1 neutralizing activity, wherein said antibody or antigen-binding portion thereof recognizes a epitope on a V1/V2 domain of HIV-1 gp120, wherein said epitope is dependent on the presence of a sequence in the V1 loop;

an isolated human monoclonal antibody produced by the hybridoma cell line selected from the group consisting of: cell line 35D10/D2 (ATCC Accession Number PTA-3001), cell line 40H2/C7 (ATCC Accession Number PTA-3006), cell line 43A3/E4 (ATCC Accession Number PTA-3005), cell line 43C7/B9 (ATCC Accession Number PTA-3007), cell line 45D1/B7 (ATCC Accession Number PTA-3002), cell line 46E3/E6 (ATCC Accession Number

PTA-3008), cell line 58E1/B3 (ATCC Accession Number PTA-3003),  
cell line 64B9/A6 (ATCC Accession Number PTA-3004), cell line  
8.22.2 (ATCC Accession Number PTA-4007), and cell line 8.27.3  
(ATCC Accession Number PTA-4012), or an antigen-binding  
portion thereof;

an isolated human antibody or antigen-binding portion  
thereof that specifically binds to HIV-1 gp120 protein and  
that has HIV-1 neutralizing activity, wherein said antibody or  
antigen-binding portion thereof recognizes a epitope on a  
V1/V2 domain of HIV-1 gp120, wherein said antibody or antigen  
binding portion thereof recognizes a linear epitope on a V2  
domain of HIV-1 gp120; and

an isolated human monoclonal antibody or antigen-binding  
portion thereof that specifically binds to an epitope on a V3  
region of HIV-1 gp120, wherein said antibody binds to an  
epitope on the V3 region of HIV-1, and wherein said antibody  
does not specifically bind to a peptide consisting of SEQ ID  
NO: 9.

119. (Amended) A method for inhibiting HIV-1 virus  
infection of a T cell comprising the step of contacting said  
virus with [an antibody according to any one of claims 1-18,  
20-23, 30-38, 40-44, 51-57, 59-70 or 77, or an antigen-binding

portion thereof] an isolated human antibody or antigen-binding portion thereof selected from the group consisting of

an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein and that has HIV-1 neutralizing activity, wherein said antibody or antigen-binding portion thereof recognizes a epitope on a V1/V2 domain of HIV-1 gp120, wherein said epitope is dependent on the presence of a sequence in the V1 loop;

an isolated human monoclonal antibody produced by the hybridoma cell line selected from the group consisting of: cell line 35D10/D2 (ATCC Accession Number PTA-3001), cell line 40H2/C7 (ATCC Accession Number PTA-3006), cell line 43A3/E4 (ATCC Accession Number PTA-3005), cell line 43C7/B9 (ATCC Accession Number PTA-3007), cell line 45D1/B7 (ATCC Accession Number PTA-3002), cell line 46E3/E6 (ATCC Accession Number PTA-3008), cell line 58E1/B3 (ATCC Accession Number PTA-3003), cell line 64B9/A6 (ATCC Accession Number PTA-3004), cell line 8.22.2 (ATCC Accession Number PTA-4007), and cell line 8.27.3 (ATCC Accession Number PTA-4012), or an antigen-binding portion thereof;

an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein and that has HIV-1 neutralizing activity, wherein said antibody or antigen-binding portion thereof recognizes a epitope on a

V1/V2 domain of HIV-1 gp120, wherein said antibody or antigen binding portion thereof recognizes a linear epitope on a V2 domain of HIV-1 gp120; and

an isolated human monoclonal antibody or antigen-binding portion thereof that specifically binds to an epitope on a V3 region of HIV-1 gp120, wherein said antibody binds to an epitope on the V3 region of HIV-1, and wherein said antibody does not specifically bind to a peptide consisting of SEQ ID NO: 9.

120. (Amended) A method of inhibiting HIV-1 gp120-mediated binding comprising the step of contacting a gp120-expressing HIV-1 virus with [an antibody according to any one of claims 1-18, 20-23, 30-38, 40-44, 51-57, 59-70 or 77, or an antigen-binding portion thereof] an isolated human antibody or antigen-binding portion thereof selected from the group consisting of

an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein and that has HIV-1 neutralizing activity, wherein said antibody or antigen-binding portion thereof recognizes a epitope on a V1/V2 domain of HIV-1 gp120, wherein said epitope is dependent on the presence of a sequence in the V1 loop;

an isolated human monoclonal antibody produced by the hybridoma cell line selected from the group consisting of: cell line 35D10/D2 (ATCC Accession Number PTA-3001), cell line 40H2/C7 (ATCC Accession Number PTA-3006), cell line 43A3/E4 (ATCC Accession Number PTA-3005), cell line 43C7/B9 (ATCC Accession Number PTA-3007), cell line 45D1/B7 (ATCC Accession Number PTA-3002), cell line 46E3/E6 (ATCC Accession Number PTA-3008), cell line 58E1/B3 (ATCC Accession Number PTA-3003), cell line 64B9/A6 (ATCC Accession Number PTA-3004), cell line 8.22.2 (ATCC Accession Number PTA-4007), and cell line 8.27.3 (ATCC Accession Number PTA-4012), or an antigen-binding portion thereof;

an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein and that has HIV-1 neutralizing activity, wherein said antibody or antigen-binding portion thereof recognizes a epitope on a V1/V2 domain of HIV-1 gp120, wherein said antibody or antigen binding portion thereof recognizes a linear epitope on a V2 domain of HIV-1 gp120; and

an isolated human monoclonal antibody or antigen-binding portion thereof that specifically binds to an epitope on a V3 region of HIV-1 gp120, wherein said antibody binds to an epitope on the V3 region of HIV-1, and wherein said antibody



does not specifically bind to a peptide consisting of SEQ ID NO: 9.

121. (Amended) The method according to any one of claims [115-120] 115 or 116, further comprising the step of administering one or more additional therapeutic agents.

123. (Amended) The method according to any one of claims [115-117 or 121] 115 or 116, wherein said administering step is performed via an intravenous, subcutaneous, intramuscular, oral, pulmonary inhalation, transdermal or parenteral route.

135. (Amended) An isolated cell line that produces [the antibody according to any one of claims 1-18, 20-23, 30-38, 40-44, 51-57, 59-70 or 77] an isolated human antibody or antigen-binding portion thereof selected from the group consisting of

an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein and that has HIV-1 neutralizing activity, wherein said antibody or antigen-binding portion thereof recognizes a epitope on a V1/V2 domain of HIV-1 gp120, wherein said epitope is dependent on the presence of a sequence in the V1 loop;

an isolated human monoclonal antibody produced by the hybridoma cell line selected from the group consisting of: cell line 35D10/D2 (ATCC Accession Number PTA-3001), cell line 40H2/C7 (ATCC Accession Number PTA-3006), cell line 43A3/E4 (ATCC Accession Number PTA-3005), cell line 43C7/B9 (ATCC Accession Number PTA-3007), cell line 45D1/B7 (ATCC Accession Number PTA-3002), cell line 46E3/E6 (ATCC Accession Number PTA-3008), cell line 58E1/B3 (ATCC Accession Number PTA-3003), cell line 64B9/A6 (ATCC Accession Number PTA-3004), cell line 8.22.2 (ATCC Accession Number PTA-4007), and cell line 8.27.3 (ATCC Accession Number PTA-4012), or an antigen-binding portion thereof;

an isolated human antibody or antigen-binding portion thereof that specifically binds to HIV-1 gp120 protein and that has HIV-1 neutralizing activity, wherein said antibody or antigen-binding portion thereof recognizes a epitope on a V1/V2 domain of HIV-1 gp120, wherein said antibody or antigen binding portion thereof recognizes a linear epitope on a V2 domain of HIV-1 gp120; and

an isolated human monoclonal antibody or antigen-binding portion thereof that specifically binds to an epitope on a V3 region of HIV-1 gp120, wherein said antibody binds to an epitope on the V3 region of HIV-1, and wherein said antibody

does not specifically bind to a peptide consisting of SEQ ID NO: 9.

137. (Amended) The hybridoma according to claim 136 that produces an antibody selected from the group consisting of 35D10/D2, secreted by a hybridoma designated by ATCC Accession Number PTA-3001, 40H2/C7, secreted by a hybridoma designated by ATCC Accession Number PTA-3006, 43A3/E4, secreted by a hybridoma designated by ATCC Accession Number PTA-3005, 43C7/B9, secreted by a hybridoma designated by ATCC Accession Number PTA-3007, 45D1/B7, secreted by a hybridoma designated by ATCC Accession Number PTA-3002, 46E3/E6, secreted by a hybridoma designated by ATCC Accession Number PTA-3008, 58E1/B3 secreted by a hybridoma designated by ATCC Accession Number PTA-3003, 64B9/A6, secreted by a hybridoma designated by ATCC Accession Number PTA-3004, 8E11/A8 secreted by a hybridoma designated by ATCC Accession Number PTA-4012, 8.27.3, secreted by a hybridoma designated by ATCC Accession Number PTA-3009 and 8.22.2, secreted by a hybridoma designated by ATCC Accession Number PTA-4007.

139. (Amended) [A] The human antibody according to claim 1 that competes with an antibody according to claim 20

for binding to an antigen bound by an antibody according to claim 20.